slow thawing to at least −30°C maximize tumor destruction.

The advantage of cryotherapy over all other methods is its simplicity. A single, inexpensive outpatient treatment is almost always sufficient. Freezing does not jeopardize the function or appearance of the eyelid, nor does it damage the lacrimal excretory ducts. Cryotherapy, surgical operation and radiation are all useful in treatment of periocular tumors. It is important to understand the advantages and limitation of each in selecting which modality to use. Best results can only be obtained with proper case selection and careful technique.

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Adenovirus Infections of the Eye

ADENOVIRUS INFECTIONS of the eye are a universal problem affecting the conjunctiva and frequently the cornea. They seldom cause serious permanent visual loss but do cause significant morbidity. Many adenovirus types sporadically infect the eye and types 3, 7, 8 and 19 have caused epidemics of keratoconjunctivitis.

Epidemic keratoconjunctivitis has been recognized since the turn of the century but became a problem in the continental United States during World War II with outbreaks of "shipyard conjunctivitis" in West Coast shipyards.

Type 8 keratoconjunctivitis illustrates the characteristic clinical appearance and course of ocular adenovirus infections. Photophobia, irritation and tearing begin abruptly, accompanied by an acute follicular conjunctivitis with occasional subconjunctival hemorrhages or pseudomembranes and frequent ipsilateral preauricular lymphadenopathy. The other eye is commonly, though less severely, infected in two to five days. The conjunctivitis resolves in two to three weeks, usually without scarring.

Vision is blurred and distorted in 50 percent of cases with corneal involvement (keratitis). Initially, the virus infects the corneal epithelium and about three weeks later typical subepithelial opacities, presumably an antibody response to the virus antigens, appear. These opacities usually clear in weeks to months though scars may persist, and occasionally there is a permanent visual loss. Corneal changes in types other than 8 and 19 are less severe and disappear more quickly.

Ocular adenovirus infections in children and type 3 infections often have associated systemic symptoms.

Diagnosis, usually clinical, is easy during an epidemic but more difficult in sporadic cases. It may take two to three weeks for a virus to grow in culture and for serum neutralizing antibody titers to rise. Direct immunofluorescence of conjunctival scrapings is a new, fast, accurate way of identifying the virus. However, these diagnostic tests require special laboratories.

Treatment of the keratoconjunctivitis is nonspecific. Uses of lubricants, astringents, cool compresses, mydriatics and antibiotics to prevent secondary infection are the mainstays of therapy. In rare cases, topical glucocorticoids are used to eliminate visually-incapacitating subepithelial infiltrates; however, it may be difficult to discontinue the administration of steroids, prolonging the course of the disease. Trifluridine inhibits replication of some adenovirus types to varying degrees in tissue culture, but there are no antiviral agents effective against adenovirus available for clinical use at present.

The recognition of possible ocular adenovirus infection and institution of appropriate measures to prevent its spread are crucial. Although the abrupt onset of redness, irritation, tearing, and photophobia unrelieved by astringents or antibiotics is often noninfectious, infection, including adenovirus, should be suspected. More than 95 percent of adults in the United States are susceptible to adenovirus type 8. The virus is spread by close contact and type 3 can be spread in swimming pools. Adenovirus has an incubation period of 5 to 12 days, is shed from the eye up to two week after the onset of symptoms, has been isolated from asymptomatic patients and survives in dried ocular secretions for a week at room temperature. Epidemics have been started in and sustained by eye care centers; adenovirus can be spread by an examiner's fingers or by infected equipment. Routine and careful washing of hands by examiners, especially after examining patients with red eyes, and cleaning diagnostic instruments after each use can prevent the spread of adenovirus. Affected staff, including physicians,

should not work for 10 to 14 days after symptoms begin. The attendent loss of income and the disruption of the practice can usually be prevented by routine care during eye examination.

We know adenovirus can cause keratoconjunctivitis. We can quickly identify it by direct immunofluorescent staining of conjunctival cells, and we can frequently prevent its spread. We are now awaiting the development of a specific antiadenovirus agent.

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HLA Antigens and Glaucoma

THE HISTOCOMPATIBILITY (HLA) SYSTEM is of immediate interest and relevance to many workers in ophthalmology. Research in this area is in an extremely active phase. Data are being collected and new information is becoming known; however, one has to be prepared for changes in views and ideas as a result of improved methods and investigations.

Associations between HLA antigens and a particular disease are characterized by relative increases in the frequency of particular antigens in the group of diseased patients as compared with racially and ethnically matched control groups. Thus, control is important as the normal frequency of certain HLA types varies considerably in various parts of the world. For example, HLA-B5 is found in 34 percent of Japanese and only 4 percent of Africans; HLA-B8 is found in 25 percent of British and 1 percent of Japanese control subjects.

Both ankylosing spondylitis and Reiter syndrome are associated with iridocyclitis and there is a statistically significant increased incidence of HLA-B27 in these systemic diseases.

Studies suggest a relationship between HLA types and recurrent corneal herpes simplex infections. Zimmerman's co-workers found that HLA-B5 was significantly increased in the group with recurrent herpes simplex virus keratitis as compared to the control group.

Inheritance of the HLA system was determined in 235 persons from 64 families with retinoblastoma and HLA antigens of 255 healthy blood donors was determined as a control group. They found an increase of HLA-BW5 antigens among the retinoblastoma patients, particularly among hereditary cases of retinoblastoma. Simultaneously, they report a decreased HLA-12 antigen frequency among both hereditary and nonhereditary retinoblastoma patients.

There is no significant deviation of any antigen which could be found in Eales disease, chorioretinitis or central serous retinopathy. However, in patients with malignant choroidal melanoma, there is a significantly higher incidence of HLA-AW32. HLA analysis in a total of 514 patients with malignant melanomas in other parts of the body failed to show any significant HLA deviation. Skepticisms are also enhanced by the fact that so far all disease-associated HLA antigens belong to the HLA-B or HLA-D locus, or both.

Aviner and co-workers reported an increased frequency of HLA-BW35 in primary open-angle glaucoma in a predominantly white patient population with a high percentage of patients of Jewish background. These authors warned that the increase was so low it might represent a chance deviation. A series of publications from Washington University in St. Louis found the frequency of B7 and B12 significantly increased in primary open-angle glaucoma.

However, Rich and associates, Dangmar and co-workers and others could show no correlation of any of the serologically studied HLA antigens with primary open-angle glaucoma.

Kass and associates from Washington University, St. Louis, enlarged their series, reviewed all their data and concluded that the associations between A and B loci of the HLA antigen system and primary open-angle glaucoma are less impressive than previously reported. At present, there is no clear-cut evidence of HLA antigens having a definite association with open-angle or angle-closure glaucoma.

In families in which there is a familial disease problem, sometimes an HLA link can be found. For example, all of the children in a family who have received their mother's HLA haplotypes will have her disease and the children that have another haplotype will be free of the disease. In this way, although a particular disease cannot be found to be linked to a particular HLA type by